CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-264

Microbiology Review(s)

Product Quality Microbiology Review
12 May 2003
Review for HFD 120

NDA	21-264 N(BI)
Drug Product Name	
Proprietary:	[redacted]
	10 mg/ml
Non-proprietary	apomorphine hydrochloride, USP
Drug Product Classification:	Standard
Review Number:	3
Subject of this Review	
Submission Date	April 25, 2003
Receipt Date	April 28, 2003
Consult Date:	May 1, 2003
Date Assigned for Review.	May 8, 2003
Submission History (for amendments only)	
Date(s) of Previous Submission(s):	April 17, 2000 and June 14, 2002
Date(s) of Previous Micro Review(s):	June 12, 2000 and March 31, 2003
Applicant/Sponsor Name:	Mylan Pharmaceuticals
Address.	781 Chestnut Ridge Road P O Box 4310 Morgantown, WV 26504-4310
Representative:	Andrea B Miller
Telephone	(304) 599-2595 ext 6869

Name of Reviewer: Stephen E Langille, Ph D

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A	1	**TYPE OF SUPPLEMENT.**	N/A
	2.	**SUPPLEMENT PROVIDES FOR**	N/A
	3	**MANUFACTURING SITES**	Draxis Pharma Inc 16751 Route Transcanadienne Kirkland (Quebec) Canada and Vetter Pharma-Fertigung GmbH & Co KG Schuetzenstrasse 87, D-88212 Ravensburg, Germany
	4	**DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY**	• Sterile solution for injection • Subcutaneous injection • 10 mg/ml • 2 mL/ampoule and 3 mL cartridge • Single dose (2 mL) and multiple dose (3 mL)
	5	**METHOD(S) OF STERILIZATION**	———
	6	**PHARMACOLOGICAL CATEGORY**	Neurophramocological agent for the treatment of late stage Parkinson's Disease
B		**SUPPORTING/RELATED DOCUMENTS**	None

C. **REMARKS** The first review of this NDA was completed on June 12, 2000 The microbiological deficiencies identified during this review were conveyed to the Applicant in a letter dated August 14, 2000 Mylan has addressed these deficiencies (volume 6) and re-submitted the same Draxis facility sterility assurance documentation that was provided in the original submission In addition, Mylan has submitted the sterility assurance information for 3 0 mL cartridge production at Vetter Pharma Fertigung The sponsor has provided a written response to the microbiology deficiencies listed in the March 31, 2003 review

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Executive Summary

I Recommendations

A Recommendation on Approvability -
Recommended for approval from the standpoint of microbial product quality

B Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

II Summary of Microbiology Assessments

A Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -
A 3 mL cartridge will be produced at Vetter Pharma Fertigung
The cartridge preserved with benzyl alcohol

B Brief Description of Microbiology Deficiencies -
No microbiological deficiencies were identified based upon the information provided

C Assessment of Risk Due to Microbiology Deficiencies -
Not applicable

III Administrative

/S/

A. Reviewer's Signature _____

B Endorsement Block
In DFS

C CC Block
In DFS

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/s/

Stephen Langille
5/14/03 02 25 16 PM
MICROBIOLOGIST

Peter Cooney
5/14/03 03 51 31 PM
MICROBIOLOGIST

Product Quality Microbiology Review
31 March 2003
Review for HFD 120

NDA:	21-264
Drug Product Name	
Proprietary:	———
Non-proprietary·	10 mg/ml apomorphine hydrochloride, USP
Drug Product Classification:	Standard
Review Number	2
Subject of this Review	
Submission Date	June 14, 2002
Receipt Date	August 14, 2002
Consult Date	August 14, 2002
Date Assigned for Review.	August 23, 2002
Submission History (for amendments only)	
Date(s) of Previous Submission(s)·	April 17, 2000
Date(s) of Previous Micro Review(s).	June 12, 2000
Applicant/Sponsor Name:	Mylan Pharmaceuticals
Address·	781 Chestnut Ridge Road P O Box 4310 Morgantown, WV 26504-4310
Representative.	Frank R Sisto
Telephone.	(304) 599-2595

Name of Reviewer: Stephen E Langille, Ph D

Conclusion: Approvable pending revision

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ON ORIGINAL

Product Quality Microbiology Data Sheet

A	1	**TYPE OF SUPPLEMENT:**	Original Submission
	2	**SUPPLEMENT PROVIDES FOR**	Not applicable
	3	**MANUFACTURING SITES**	Draxis Pharma Inc 16751 Route Transcanadienne Kirkland (Quebec) Canada and Vetter Pharma-Fertigung GmbH & Co KG Schuetzenstrasse 87, D-88212 Ravensburg, Germany
	4	**DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY**	• Sterile solution for injection • Subcutaneous injection • 10 mg/ml • 2 mL/ampoule and 3 mL cartridge • Single dose (2 mL) and multiple dose (3 mL)
	5	**METHOD(S) OF STERILIZATION**	—
	6	**PHARMACOLOGICAL CATEGORY**	Neurophramocological agent for the treatment of late stage Parkinson's Disease
B		**SUPPORTING/RELATED DOCUMENTS**	None
C		**REMARKS**	The first review of this NDA was completed on June 12, 2000 The microbiological deficiencies identified during this review were conveyed to the Applicant in a letter dated August 14, 2000 Mylan has addressed these deficiencies (volume 6) and re-submitted the same Draxis facility sterility assurance documentation that was provided in the original submission In addition, Mylan has submitted the sterility assurance information for 3 0 mL cartridge production at Vetter Pharma Fertigung

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APPEARS THIS WAY
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Executive Summary

I. Recommendations

A Recommendation on Approvability -

The submission is approvable pending the resolution of microbiological deficiencies

B Recommendations on Phase 4 Commitments and/or Agreements, if Approvable -

II Summary of Microbiology Assessments

A Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology -

A 3 mL cartridge will be produced at Vetter Pharma Fertigung
The cartridge — preserved with benzyl alcohol

B Brief Description of Microbiology Deficiencies -

The microbiological deficiencies identified at the Vetter Pharma Fertigung facility include

- —
- —
- —
- —
- —

C Assessment of Risk Due to Microbiology Deficiencies -

Failure to address the microbiological deficiencies outlined above will increase the risk of drug product contamination

III Administrative

/S/

A Reviewer's Signature _____

B Endorsement Block

In DFS

C CC Block

In DFS

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/s/

Stephen Langille
4/8/03 03 17 43 PM
MICROBIOLOGIST

Peter Cooney
4/9/03 08 53 00 AM
MICROBIOLOGIST

COMPLETED JUN 13 2000

REVIEW TO HFD 120
OFFICE OF NEW DRUG CHEMISTRY
Microbiology Staff, HFD-805
Microbiologist's Review #1 of Original NDA
May 31, 2000

JUN 12 2000

A	1	NDA	**21-264**
	2	APPLICANT/SPONSOR	**Mylan Pharmaceuticals** **781 Chestnut Ridge Road** **P O Box 4310** **Morgantown, WV 26504-4310**
		Contact	**Frank R. Sisto** **Vice President, Regulatory Affairs** **(304) 599-2595**
	3	MANUFACTURING SITE	**Draxis Pharma Inc** **16751 Route Transcanadienne** **Kirkland (Quebec) Canada**
	4	DRUG PRODUCT NAME	
		Proprietary	**— 10 mg/ml**
		Nonproprietary	**apomorphine hydrochloride, USP**
		Drug Priority Classification	**Standard**
	5	DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY	• **Sterile solution for injection** • **Subcutaneous injection** • **10 mg/ml** • **2 mL/ampoule** • **Single dose**
	6	METHOD(S) OF STERILIZATION	—
	7	PHARMACOLOGICAL CATEGORY AND/OR PRINCIPLE INDICATION	**Neurophramocological agent for the treatment of late stage Parkinson's Disease**

B 1 DOCUMENT/LETTER DATE. **April 17, 2000**
2 RECEIPT DATE. **May 1, 2000**
3 CONSULT DATE. **April 28, 2000**
4 DATE OF AMMENDMENT.
5 ASSIGNED FOR REVIEW. **May 11, 2000**
6 SUPPORTING/RELATED DOCUMENTS

C REMARKS This is an original NDA seeking approval for an orphan drug product Contract manufacturing will take place at Draxis Pharma Inc Kirkland, Quebec, Canada

D CONCLUSIONS The submission is approvable pending resolution of microbiological deficiencies Specific comments regarding the [redacted] are provided in "E Review Notes" and "List of Microbiology Deficiencies and Comments"

Stephen E Langille, Ph D

6/12/00

cc Original **NDA 21-264**
HFD-120/Division File
HFD-120/CSO/Wheelous
HFD 805/Consult File/Langille
Drafted by S Langille v microrev\# 21-264r1
Initialed by P Cooney

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